Alcohol Consumption Protects against Arthritis Development in Seropositive Arthralgia Patients

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INTRODUCTION

Patients with arthralgia and auto-antibodies such as anticitrullinated protein antibodies and/or IgM–rheumatoid factor (seropositive) are at risk for developing rheumatoid arthritis (RA). RA is associated with lower alcohol intake, suggesting that alcohol consumption is protective for the development of RA. The proposed mechanism for this effect is that alcohol is immunosuppressive, possibly via intrinsic corticosteroid production. In animal models several immunosuppressive effects have been found and in humans alcohol intake also causes immune modulation. However, cross-sectional studies on the effect of alcohol on RA risk are hampered by multiple confounding factors. For instance, pain, psychological distress and the use of disease modifying antirheumatic drugs may be associated with both RA and alcohol consumption. Such factors can only be avoided by studying an at-risk population prospectively.

METHODS

We have prospectively followed 361 seropositive arthralgia patients, without clinical signs of arthritis, for the development of arthritis. The study was approved by the local ethics committee and all patients gave informed consent. Patients were followed for a median of 32 months. Hundred and twenty-six (35%) patients developed arthritis after a median follow-up of 12 months, of whom 116 (92%) were diagnosed with RA according to the 2010 ACR/EULAR criteria.

RESULTS

Cox regression analysis showed that alcohol consumption at baseline was inversely related with the risk of development of arthritis (table 1). Analysis with alcohol as a categorical variable showed that this was not a linear relation. Rather, the consumption of alcohol per se was protective for the development of arthritis. When moderate drinkers were compared with regular drinkers, no significant association was found. This indicates that the consumption of alcohol is protective against the development of arthritis in seropositive arthralgia patients, with an equal effect of moderate or large amounts of alcohol. An explanation for this phenomenon can be that often U shaped relations are found between alcohol consumption and inflammatory markers. With higher quantities of alcohol, the beneficial effects could therefore equal the detrimental effects, resulting in an equal risk of the development of arthritis of moderate and high alcohol quantities. Patients
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Consuming alcohol had a lower pain visual analog scale (VAS) than non-consumers (median 30; IQR: 10–50 and 40; IQR: 14–60, respectively), although this association was not significant (p=0.06).

**Table 1 Association of alcohol consumption with risk of arthritis development in seropositive arthralgic patients**

<table>
<thead>
<tr>
<th>Alcohol intake</th>
<th>Number of persons at risk</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Units/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Categorical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never (0 units)</td>
<td>132</td>
<td>Reference group</td>
</tr>
<tr>
<td>Sometimes (0–&lt;1 unit)</td>
<td>123</td>
<td>0.64 (0.42 to 0.98)*</td>
</tr>
<tr>
<td>Regularly (≥1 unit)</td>
<td>106</td>
<td>0.57 (0.36 to 0.90)*</td>
</tr>
<tr>
<td>Binominal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>132</td>
<td>Reference group</td>
</tr>
<tr>
<td>Yes</td>
<td>229</td>
<td>0.61 (0.42 to 0.88)*</td>
</tr>
</tbody>
</table>

* p Value<0.05; unit: 250 ml beer, 125 ml wine or 35 ml spirit.

Confounding analysis (ΔB>10%) revealed shared epitope (SE) status as a confounder for the relation of alcohol with the development of arthritis. Age, sex, smoking, ethnicity, anti-Cyclic Citrullinated Peptide (aCCP) rheumatoid factor, C reactive protein, VAS pain and non-steroidal anti-inflammatory drugs use were not confounders. Since the analysis for confounding does not discriminate between confounding and mediation, these results could indicate that SE status is a mediator for the effect that alcohol has on the risk of developing arthritis. This association is in line with animal studies showing that alcohol consumption has a suppressive effect on Major Histocompatibility Complex class II (MHCII) expression of B cells.\(^\text{10}\)

Part of the immunosuppressive effect that alcohol has could thus be via a lower expression of SE containing MHCII molecules.

**CONCLUSION**

In conclusion, alcohol consumption seems to protect against the development of arthritis in seropositive arthralgia patients and this effect might partly be mediated via SE expression.

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REFERENCES


